REMARKS

Claims 1-9, 11-18, and 21 are of record in this application. No claims have been amended. Claims 10, 19, and 20 have been canceled, and new claim 21 has been added.

Support for new claim 21, drawn to *Streptococcus agalactiae* isolated from infected fish, is inherent in the original disclosure, such as at lines 4-7 of paragraph no. 0023, bridging pages 7 and 8.

Claim Status

Applicants note that dependent claims 3, 5, and 15 have not been rejected over prior art. Applicants respectfully request clarification of the status of these claims. Specifically, is the Examiner of the belief that these claims are free of the prior art and would be patentable if placed in independent form incorporating all of the limitations of the claims from which they depend, and if the rejections under 35 U.S.C. 112 were either overcome or withdrawn?

Restriction Requirement

Applicants hereby affirm the election of claim Group I, claims 1-9 and 11-18. Applicants' traversal of this restriction

was on the basis that the search for any one group would have been co-extensive for the others, and that an examination of all claims would not have entailed a serious burden. However, to expedite prosecution, the non-elected claims 10, 19, and 20 have been canceled.

Objection to the Disclosure

The Examiner has objected to the Figures because it is not clear what the symbols represent. In reply, Applicants note that the symbols are described in the specification at paragraph no. 0015 on page 5. If the pages of the Figures are distorted or illegible such that the symbols in the Figures are not clear, Applicants will resubmit substitute pages of the Figures at the Examiner's request.

Rejection Under 35 U.S.C. 112

Claims 5-9, 17, and 18 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Each of the issues raised by the Examiner is addressed hereinbelow.

A. The Examiner has indicated that claim 5 is indefinite in the use of the phrase "substantially free". Applicants respectfully disagree.

It is well established that the use of relative terms does not automatically render a claim invalid. A discussion of the factors to be considered when applying 35 U.S.C. 112 to the use of "substantially" was provided by the CAFC in *Seattle Box Co. v. Industrial Crating & Packing, Inc.* (CAFC 1984) 221 USPQ 568. In *Seattle*, the CAFC held that the use of "substantially" was not indefinite, stating that:

> "When a word of degree is used the district court must determine whether the patent's specification provides some standard for measuring that degree. The trial court must decide, that is, whether one of ordinary skill in the art would understand what is claimed when the claim is read in light of the specification."

The Court further held that the specification need not set precise limits, and that the claims are patentable under §112 even if some experimentation was required to determine the limits of the claims (page 574). Reaching a similar conclusion, the CCPA held that the use of substantially was not indefinite under §112 in *In re Mattison and Swanson* (CCPA 1975) 184 USPQ 484. As described therein, the CCPA concluded that neither the claims nor the specification need specify numerical limits for what was considered "substantial". Rather, the specification need only

set forth general guidelines sufficient to allow a skilled practitioner to make a proper choice of the claimed components:

> "Hypothesizing whether an increase in efficiency of 3%, 30%, or 300% is necessary for said increase to be classified as substantial is not determinative of the issue of whether the claims satisfy 35 U.S.C. 112, second paragraph."

See also *In re Swinehart and Sfiligoj* (CCPA 1971) 169 USPQ 226, 230, and the more recent *Liquid Dynamics Corp. v. Vaughan Co.* (CAFC 2004) 69 USPQ2d 1595.

Returning to the claims at issue, the specification discloses that the vaccine is a combination of a killed cell preparation of *S. agalactiae* together with a concentrated fraction of the extracellular filtrate of a culture of *S. agalactiae*. It is this concentrated fraction which is substantially free of cells, cell wall fragments, and intracellular components of *S. agalactiae* (lines 1-6 of paragraph no. 0024 on page 8). Applicants are of the belief that various low molecular weight components of the extracellular products of killed *S. agalactiae* have an inhibitory effect upon the antigenicity of the bacterin suspensions. Thus, concentration and filtration of the extracellular retentate substantially removes these inhibitory components and thus increases efficacy of the vaccine. In addition, the extracellular products are also believed to include antigens from the capsule or

secreted/excreted antigens and other beneficial molecules providing a superior immunization response (lines 17-26 of paragraph no. 0024, pages 8-9).

The specification further discloses, at lines 6-17 of paragraph no. 0024, that:

> "Although the cells are removed from the concentrated fraction, **the skilled practitioner will recognize that a relatively small amount of intracellular products and cell wall fragments may be present as the result of normal cell lysis occurring during the course of culture**" (emphasis added).

Thus, the application clearly describes the basis for the presence of small amounts of contaminating intracellular products and cell wall fragments, and their relationship to the term in question. Applicants therefore submit that a practitioner skilled in the art would fully understand what is intended by the claims and could readily determine their scope. It is not necessary to set forth the precise degree of purity intended by "substantially free".

B. Claims 6-9, 17, and 18 have been rejected as indefinite in reciting a "molecular weight greater than about 1 (or 2 or 3) kDa." The Examiner has questioned how this was determined. Applicants respectfully disagree.

The designation of molecular weight in units of kilodaltons or kDa is well known and is the art recognized standard. These units are used in a myriad of textbooks and publications throughout the chemical and biological sciences, as well as in commerce. Applicants submit that a practitioner skilled in the art would have no difficulty understanding the claim or determining its scope; the skilled practitioner would not require a description of how the molecular weight was determined to understand the claim. Moreover, for the sake of argument, Applicants note that the specification, at paragraph no. 0028 on pages 11-12, discloses that the cell-free culture fluid may be filtered to remove low-molecular weight components by use of filters having molecular weight cut-offs of 1, 2 or 3 kDa, and further describes preferred commercially available filtration systems. Likewise, Example 1, paragraph no. 0039 on pages 17-18 discloses removing low molecular weight components using a 2 kDa hollow fiber filter concentrator.

Rejection Under 35 U.S.C. 112

Claims 3 and 15 have been rejected under 35 U.S.C. 112, first paragraph, as failing to provide an enabling disclosure. The Examiner has indicated that deposits of the claimed strains

of *Streptococcus agalactiae* do not indicate the extent of public availability.

In response, the disclosed and claimed strains of *S. agalactiae* designated ARS-KU-3 B and ARS-KU-11 B were deposited under the provisions of the Budapest Treaty in the Agricultural Research Service Culture Collection (NRRL), 1815 N. University St., Peoria, IL, 61604, USA, on July 17, 2002, and were assigned Deposit Accession Nos. NRRL B-30608 and NRRL B-30607, respectively. These deposits are referred to in the specification at paragraph no. 0018 on page 6.

Applicants' representative, Randall E. Deck, further states that in addition to the deposits meeting the terms of the Budapest Treaty:

(1) all restrictions on the availability of the deposits will be irrevocably removed upon the granting of the patent, and

(2) the deposits will be replaced if they should become non-viable.

Defective Oath or Declaration

The Examiner has indicated that the oath was not executed. In response, Applicants note that duly executed Declarations were

submitted to the PTO on July 19, 2004, in the Reply to Notice to File Missing Parts of Nonprovisional Application. A copy of this Reply, together with Applicants' stamped Post Card Receipt is enclosed herewith.

Rejection Under 35 U.S.C. 102

Claims 1, 2, 4, and 6-9 have been rejected under 35 U.S.C. 102(e) as being anticipated by Norcross *et al.* Applicants respectfully disagree.

Norcross *et al.* (hereinafter referred to as Norcross) discloses a vaccine for the prevention of mastitis in cows. The disclosed vaccine includes killed cells of *Staphylococcus aureus* [encapsulated and/or non-encapsulated, paragraphs (a) and (b) in column 6], four toxoids of *Staphylococcus aureus* [paragraphs (c), (d), (e), and (f) in column 6], **and killed cells (*i.e.*, bacterin) of *Streptococcus agalactiae* [paragraph (g) in column 6].** The preparation of the *Streptococcus agalactiae* containing vaccine is disclosed in Example III, at lines 55-68 of column 21. As disclosed therein, the *S. agalactiae* was grown, and the cells were harvested (separated from the culture medium) "by centrifugation at g and washed in sterile saline." The isolated, washed cells were then inactivated (killed), washed again, and

administered to the subject animals. The reference does not disclose combining the killed cells with a concentrated extract of a culture of β-hemolytic *Streptococcus agalactiae*, nor does it disclose using *Streptococcus agalactiae* which are β-hemolytic.

The instant invention is drawn to vaccines effective for the control of *Streptococcus agalactiae* in fish. The vaccines comprise two components: (1) intact (whole) killed cells of one or more β-hemolytic isolates of *Streptococcus agalactiae*, and (2) the concentrated extract from a culture of a β-hemolytic *Streptococcus agalactiae*. As disclosed at paragraph no. 0024 on pages 8-9, this concentrated extract is prepared from the extracellular filtrate (cell-free culture fluid) of a culture of *S. agalactiae*. As such, the concentrated fraction is substantially free of cells, cell wall fragments, and intracellular components of *S. agalactiae*. This is not disclosed or suggested by the prior art of record.

With respect to claim 1 of record, the claim is limited to a two-part composition of (1) intact killed cells of β-hemolytic *S. agalactiae*, **and (2) a concentrated extract from a culture of a β-hemolytic *S. agalactiae***. This is not disclosed or suggested by Norcross. Indeed, Norcross expressly discloses that the cells

of *S. agalactiae* are separated from the culture medium in which they were grown and washed multiple times. Thus, not only would there not be any concentrated extract in the vaccine of Norcross, but there would not be any extracellular products present at all. Any extracellular products would have been washed away.

In addition to failing to anticipate the claimed invention, Applicants also submit that the prior art would not provide any motivation for a practitioner of ordinary skill in the art to modify the vaccine of Norcross to arrive at the claimed invention. At no point does Norcross disclose, suggest, or even mention the use of a concentrated extract from a culture of a β-hemolytic *S. agalactiae*. In the absence of such a teaching, the skilled practitioner would have no reason to add a concentrated extract from a culture of a β-hemolytic *S. agalactiae* to the vaccine of Norcross.

Rejection Under 35 U.S.C. 103

Claims 1, 2, 4, 6-9, 11-14, and 16-18 have been rejected under 35 U.S.C. 103 as being obvious over Norcross in view of Evans *et al.* (2002). The Examiner has taken the position that it would have been obvious to administer the vaccine of Norcross to

fish since Evans teaches that *S. agalactiae* is a pathogen of fish. Applicants respectfully disagree.

Norcross and the instant invention were described *supra*.

Evans *et al.* (hereinafter referred to as Evans) discloses that β-hemolytic *S. agalactiae* were isolated from and identified as pathogens of two fish species. Evens did not disclose or suggest any measures for controlling or preventing the disease, much less any vaccines or how such vaccines might be prepared.

Applicants submit that the secondary reference, Evans, does nothing to alleviate the deficiencies of the Norcross disclosure discussed in the response to the 35 U.S.C. 102 rejection, *supra*. Specifically, Evans provides nothing which would suggest the addition of a concentrated extract of a culture of β-hemolytic *S. agalactiae* in the vaccine of Norcross. Again, the skilled practitioner would have no motivation to add this concentrated extract to the vaccine of Norcross.

In addition to the arguments above, Applicants respectfully disagree with the Examiner's position that it would have been obvious to use the vaccine of Norcross in fish. The vaccine of Norcross was disclosed for treating mastitis in cows. However, it is well established that obviousness requires that the prior art provide at least some predictability or a reasonable

expectation of success of the claimed process. See *In re Gangadharam* (CAFC 1989) 13 USPQ2d 1568, *In re Whiton* (CCPA 1970) 164 USPQ 455, and *In re Rinehart* (CCPA 1976) 189 USPQ 143. Contrary to the Examiner's conclusion, a practitioner skilled in the art could not predict or expect with any reasonable degree of certainty that the vaccine of Norcross, which was disclosed for use in cows, would be effective for protecting fish. In the absence of such a reasonable expectation of success, there would be no motivation for the skilled practitioner to modify the teachings of the references as suggested by the Examiner.

Furthermore, it is generally recognized that a technique or agent which is established for use in one animal species may, at best, only be reasonably predicted to work in a different species, when the first animal is an accepted model for the second species. If it is not an accepted model, the two species cannot be reasonably predicted to respond in a similar fashion. In the instant fact situation, the cows of Norcross are obviously markedly different animals than fish. The Examiner has not provided any evidence that cows are an accepted model for fish. The significant differences between cows and fish are particularly evidenced by their classification into different classes (*i.e.*, in the taxonomic order of classification, phyla -

superclass → class → order → family → genus → species, fowl belong to the superclass *Pisces*, cows belong to the class *Mammalia*). In view of their fundamental differences, a practitioner of ordinary skill in the art would have no basis to predict that swine and fowl would react to a vaccine in a similar manner, *i.e.*, that it would be effective in fish.

For the reasons stated above, claims 1-9, 11-18, and 21 are believed to distinguish over the prior art and satisfy the requirements of 35 U.S.C. 112. Allowance thereof is respectfully requested.

Respectfully submitted,

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Enclosures
1. Reply to Notice to File Missing Parts of Nonprovisional Application with accompanying executed Declarations, July 19, 2004 (7 pages).
2. Post Card Receipt of said Reply to Notice to File Missing Parts of Nonprovisional Application (1 page).